

Remarks

Claim amendments

Claims 1, 5-12, 15, 17, and 21-32 are herein amended, claim 45 is cancelled, and claims 46 and 47 are new (from original claims 28 and 32, respectively). All amended claims reflect changes in plurality of words (molecule vs. molecules; ligand vs. ligands), or particular terms (determining a quantity of vs. obtaining a measure of), made to provide proper antecedent bases for the terms in dependent claims, and to clarify. For example, claim 1 is amended to delete “one or more target molecules” and insert “a target molecule” since both versions allow one or more target molecules, but the amended version provides proper antecedent basis for later dependent claims referring to “the target molecule.” Moreover, claims 5, 6, 8, 10, 25 and 26 have corrected the grammar from “molecules include” to “molecule includes.”

Claims 9 and 12 are amended the Markush language to properly recite “the group consisting of” rather than “*a* group consisting of.” Claim 15 is amended to read “first sample” to properly depend from claim 1. Claims 21, 23, 29, 30 and 31 are amended to correct “obtaining a measure” or “determining a concentration” to correlate to the language set forth in claim 1 – namely, “determining a quantity.”

All of the above amendments represent amendments to clarify, correct grammar, and provide proper, consistent antecedent bases for all terms in dependent claims. No new matter is added with these amendments.

Claims 28 and 32, originally multiple-dependent claims from claims 24-27, and claims 30 or 31, respectively, are amended to (a) remove the dependency from claim 26 (claim 28) and add a new dependent claim which depends only from claim 26 (claim 46);

or (b) to remove the dependency from claim 31 (claim 32) and add a new dependent claim which depends only from claim 31 (claim 47). These amendments are strictly amendments in form, to separate out dependent claims that cannot be properly claimed using the antecedents contained in the multiple-dependent claims, as originally written. No new matter is added with these amendments.

Claim 31 is amended to delete the phrase “or to multiple substrates wherein each substrate is contained in a separate chamber” because this phrase is redundant with the immediately preceding phrase “an immobilized ligand wherein the ligand is immobilized by attachment to a substrate in a single chamber” (now amended to “an a plurality of immobilized ligand ligands wherein the each ligand is immobilized by attachment to a substrate in a single chamber” to properly recite antecedents in claim 1). As originally written, an immobilized ligand attached to a substrate in a single chamber is no different from an immobilized ligand attached to multiple substrates, each substrate contained in a separate chamber. The effect is the same – a single chamber with a ligand immobilized to a substrate. Support for this deletion amendment, and the amendment to a “plurality of ... ligands, each ... immobilized to...” is found in Figs. 3 and 4, and the text accompanying Figs. 3 and 4, which is Examples G and H, pp. 18-22. Applicants respectfully submit that no new matter is added with these amendments.

Objections to Claims and Rejections based on 35 U.S.C. § 112, para. 2 – Indefiniteness

With the above-described amendments to the claims, and cancellation of claim 45, Applicants respectfully submit that all claim objections and claim rejections based on

indefiniteness have been addressed. Applicants respectfully request withdrawal of the claim objections and rejections for indefiniteness based on 35 U.S.C. § 112, para. 2.

Prior art rejections under 35. U.S.C. § 103 (a)

The core rejection of claims 1-2, 5-8, 13-24 and 33 (45 is cancelled) as being unpatentable over Dodge et al. (US2002/0051974) in view of Freytag et al. (*Clin. Chem.* **30**, 417-420, 1984 – hereinafter “Freytag 1”) for reasons of obviousness, fails because of two important distinctions. First, Dodge discloses that a) a capture molecule initially binds to the target molecule in the sample to form a capture molecule-target molecule complex, and then b) a detector molecule binds to the target molecule-capture molecule complex. As seen in claim 1 of the instant application, embodiments of the presently claimed invention require adding only “a preparation of a nucleic acid aptamer specific for each the target molecule” to the sample; then “allowing substantially all of the target molecules molecule in the first sample to bind with the aptamer” to form an aptamer-target molecule complex; and then “separating unbound aptamer from the first sample” by contacting the aptamer-target molecule complex so formed “with immobilized ligand, thereby binding the ligand to unbound aptamer, so as to recover a second sample of aptamer bound to target molecule;” and finally “using a quantitative replicative ... to determine a quantity of aptamer specific for the target molecule” Absolutely nowhere is there a requirement for a capture molecule-target molecule complex before binding an aptamer.

Second, although Dodge discloses that the detector molecule can be any aptamer (DNA oligonucleotide), Dodge specifically shows in Fig. 1A that the probe has a

fluorescent reporter dye/quencher pair such that the reporter only fluoresces upon incorporation of the probe into amplified PCR product; Dodge specifically states in para. [0068] that “the probe preferably has a 5’ reporter dye and a downstream 3’-quencher dye covalently bonded to the probe which allows fluorescent resonance energy transfer; and Dodge discloses examples of the aptamer detector molecule (Example 1) as using only oligonucleotide probes having reporter dye/quencher pairs (5’-FAM...TAMRA-3’) – see para. [0105], [0108], [0111].

There is no motivation to combine the references of Dodge and Freytag 1, and no suggestion in either reference to modify Dodge to incorporate the methodologies of Frytag, or eliminate the need for a capture molecule-target molecule-detector molecule ternary complex to that of the presently claimed binary complex of only aptamer bound to target molecule.

Without the primary rejection based on Dodge and Freytag 1, no other obviousness rejection based on additional references combined with the core Dodge and Freytag 1 combination holds water. Applicants also respectfully submit that the present references add nothing to those which have been cited in previous office actions and rebutted in previous responses.

Applicants respectfully submit that all claims are in condition for allowance and therefore request withdrawal of all rejections under 35 USC § 103(a) for reasons of obviousness.